

REMARKS / ARGUMENTS

The Claims

Claims 1-22 are currently pending in the application and Claims 1, 3-16 and 21 have been provisionally elected. Applicants have cancelled without prejudice Claims 1-22 and reserve the right to pursue claims of corresponding subject matter in subsequently filed applications.

Applicants have added new claims 23-40. The new claims are fully supported by the specification as filed and do not introduce new matter or raise new issues requiring further consideration and/or search.

Applicants respectfully request entry of the new claims.

The Restriction Requirement

The Examiner has required restriction under 35 U.S.C. 121:

- I. Claims 1, 3-21, drawn to Method for treating Lytic Bone Disease, classified in class 424, subclass 572.
- II. Claims 2, 4-12, 15-21, drawn to Method for treating/preventing Cancer Metastasis, classified in class 424, subclass 572.
- III. Claim 22, drawn to Method for treating/preventing Myeloma, classified in class 424, subclass 572.

In addition, the Examiner has required an election of species within Group I or Group II:

Group I

- Species A - Radiation
- Species B - Chemotherapy
- Species C - Antibodies
- Species D - Non-antibody polypeptides

Group II

- Species A - Radiation
- Species B - Chemotherapy
- Species C - Antibodies
- Species D - Non-antibody polypeptides

The undersigned, in a telephone conversation with Examiner Tedeschi on November 30, 2000, provisionally elected with traverse the invention corresponding to Group I, Claims 1, 3-16 and 21, and Species B. It is maintained that restriction of Groups I and II to different species of cancer therapy agents would place upon the Applicants undue burden and expense to prosecute each species separately. It is requested that the Examiner withdraw the requirement to elect a species of cancer therapy agents.

Notwithstanding the above, Applicants affirm the election under 35 U.S.C. 121 and acknowledge that the non-elected claims are being withdrawn from further consideration.

Rejections under 35 U.S.C. 102

Claims 1, 3, 5 and 8-16 are rejected under 35 U.S.C. 102(b) as being anticipated by PCT publication no. WO97/23614. Claims 1, 5, 8-10 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Simonet et al. (Cell 89, 309-319 (1997)).

New claims 22-39 are directed to methods of preventing or treating bone loss resulting from lytic bone disease and abnormal bone formation comprising administering an OPG polypeptide and a cancer therapy agent. In addition, Claim 39 is directed to dosages of from about 0.1mg/kg to about 10mg/kg. It is requested that the rejections be withdrawn.

Rejections under 35 U.S.C. 103

Claims 1, 3-16 and 21 are rejected under 35 U.S.C. 103(a) as being obvious over Boyle et al. (cited above) in view of Conte et al. (Annals of Oncology 5, S41-S44 (1994)). Claims 3, 4, 6, 7, 11-16 and 21 are rejected under 35 U.S.C. 103(a) as being obvious over Simonet et al. (cited above) in view of Conte et al. Applicants disagree.

Whether claimed subject matter is obvious under 35 U.S.C. 103 requires, *inter alia*, consideration of whether there would have been some suggestion or motivation in the cited references themselves to support combining the references to produce the claimed invention. *In re Fine* 5 USPQ2d 1598 (Fed. Cir. 1988). In the present rejection, the Examiner has not pointed out any suggestion in the references to administer an OPG polypeptide and a cancer therapy agent for treating bone loss due to cancer. The general suggestion in the Conte reference that the majority of patients with certain cancers develop lytic bone metastases does not suggest the use of OPG and chemotherapy agents for lytic bone disease. In addition, the assertion that the Conte reference generally discloses the use of bone loss inhibitors with chemotherapy in breast cancer patients does not suggest the use of OPG and chemotherapy, as one skilled in the art is not specifically directed by the reference to use OPG as a bone loss inhibitor. Applicants request that the rejection be withdrawn.

Rejections under 35 U.S.C. 112

Claims 1, 3-7, 12-16 and 21 are rejected as the subject matter is not enabled by the specification. The Examiner argues that the use of "unfused" OPG or fragments thereof to prevent and treat bone loss or lytic bone disease is not enabled and therefore the Applicants are not entitled to the scope of protection being sought. Applicants disagree.

Applicants point out that "unfused" OPG (which is taken to mean an OPG polypeptide, or fragment thereof, which is not attached to a different amino acid sequence, such as an Fc region of an immunoglobulin constant domain) and fragments thereof are active in preventing osteoclast formation as shown in Table I on p. 129 of PCT publication no. WO97/23614. One skilled in the art would readily appreciate from these teachings that unfused OPG could be used to prevent and treat bone loss, including lytic bone disease. See also p. 3, line 25 to p. 4, line 4 of the present application.

The specification enables the uses of unfused OPG as claimed since one skilled in the art could practice the invention in a manner similar to that described for OPG fused to Fc regions. Examples 2-4 of the specification may be carried out using unfused OPG polypeptides as well as OPG fusion polypeptides.

The specification shows two examples of the prevention of bone loss due to metastatic cancer and it is submitted that these examples enable the prevention of bone loss associated with cancer by administration of OPG. The Examiner argues that "tumors are significantly progressed before they become discernible", suggesting that only treatment, and not prevention, would be realistic. Applicants disagree. As was shown in the application, prevention of bone loss was shown by administering OPG to a patient having cancer which has not metastasized to bone. In this manner, OPG administration prevents bone loss should the cancer subsequently metastasize.

Applicants request that the rejection be withdrawn.

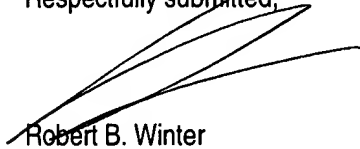
Claims 1, 3-16 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Applicants submit that new Claims 22-39 particularly point out and distinctly claim the subject matter. Withdrawal of the rejection is requested.

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CONCLUSION

Claims 23-40 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

- (b) ala-ala-ala-ala (SEQ ID NO: 9);.
- (c) ala-ala-ala-ala-ala (SEQ ID NO: 10);.
- (f) gly-gly-gly-gly-gly (SEQ ID NO: 11);.
- (g) gly-gly-gly-gly-gly-gly (SEQ ID NO: 12);.
- (i) gly-gly-pro-gly-gly (SEQ ID NO: 13);.
- (k) ser-gly-gly-gly-gly-gly-gly-gly (SEQ ID NO: 14);.
- (l) gly-gly-ser-gly-ser-gly-ala-gly-ser-gly-ser-gly-gly-gly-ser-gly-ser-gly-gly (SEQ ID NO: 15);.